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STIC


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=> d que stat l4
L1          4360 SEA FILE=HCAPLUS ABB=ON  (RSV? OR ?RESPIRATOR?(W)?SYNCYTIAL?(W)
                 ?VIRUS?)
L2           187 SEA FILE=HCAPLUS ABB=ON  L1 AND ?IMMUNOGEN?
L3           138 SEA FILE=HCAPLUS ABB=ON  L2 AND (F OR G OR M OR SH OR NS1? OR
                 NS2? OR P)
L4            13 SEA FILE=HCAPLUS ABB=ON  L3 AND M2?

=> d ibib abs l4 1-13

L4   ANSWER 1 OF 13  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:625764  HCAPLUS
TITLE:                    Evaluation of recombinant respiratory
                          syncytial virus gene deletion
                          mutants in African green monkeys for their potential
                          as live attenuated vaccine candidates
AUTHOR(S):                Jin, Hong; Cheng, Xing; Traina-Dorge, Vicki L.; Park,
                          Hyun Jung; Zhou, Helen; Soike, Ken; Kemble, George
CORPORATE SOURCE:         MedImmune Vaccines Inc., 297 North Bernardo Avenue,
                          Mountain View, CA, 94043, USA
SOURCE:                   Vaccine (2003), 21(25-26), 3647-3652
                          CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER:                Elsevier Science Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Towards the goal of developing live attenuated respiratory
     syncytial virus (RSV) vaccines to prevent
     severe respiratory tract infections caused by respiratory
     syncytial virus, recombinant RSV contg. a
     deletion of single or multiple NS1, NS2, SH
     and M2-2 genes have been generated.  In this study,
     recombinants, rA2.DELTA.M2-2, rA2.DELTA.NS2,
     rA2.DELTA.NS1NS2, rA2.DELTA.SHNS2, rA2.DELTA.M2-2NS2
     were evaluated in African green monkeys (AGMs) for their infectivity,
     immunogenicity and protection against wild type (wt) RSV
     challenge.  Replication of rA2.DELTA.NS2 and rA2.DELTA.SHNS2 was
     not attenuated in either the upper or the lower respiratory tracts of
     AGMs.  On the other hands, rA2.DELTA.NS1NS2 was over-attenuated;
     it did not replicate in the respiratory tracts of the infected monkeys and
     did not provide sufficient protection against wild type RSV
     challenge. rA2.DELTA.M2-2NS2 was slightly more attenuated than
     rA2.DELTA.M2-2 and provided partial protection against wt
     RSV challenge. rA2.DELTA.M2-2, and possibly rA2.DELTA.
     M2-2NS2, exhibited the attenuated but protective phenotypes in the
     monkeys that could be further evaluated as potential live attenuated
     RSV vaccine candidates in the clin. studies.

L4   ANSWER 2 OF 13  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:511167  HCAPLUS
DOCUMENT NUMBER:          139:51610
TITLE:                    Immunogenic compositions comprising an
                          antigen and a purified M protein from
                          respiratory syncytial virus
INVENTOR(S):              Barber, Brian; Cates, George; Parrington, Mark;
                          Sambhara, Suryprakash
PATENT ASSIGNEE(S):       Aventis Pasteur Limited, Can.
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
```

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053464	A1	20030703	WO 2002-CA1953	20021218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-341422P P 20011220

AB Methods and compns. for enhancing an immune response to an antigen in a host are provided. **Immunogenic** compn. comprising an antigen and an amt. of purified **M** protein from **respiratory syncytial virus** are provided in a pre-selected amt. to provide an enhanced immune response to said antigen in a host having a pre-existing **respiratory syncytial virus** **M**-specific immune response. The antigen can be an antigen from **respiratory syncytial virus**.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:869921 HCAPLUS
DOCUMENT NUMBER: 138:135888
TITLE: Recombinant **Respiratory syncytial virus** with the **G** and **F** genes shifted to the promoter-proximal positions
AUTHOR(S): Krempl, Christine; Murphy, Brian R.; Collins, Peter L.
CORPORATE SOURCE: Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892-8007, USA
SOURCE: Journal of Virology (2002), 76(23), 11931-11942
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The genome of human **respiratory syncytial virus** (**RSV**) encodes 10 mRNAs and 11 proteins in the order 3'-**NS1**-**NS2**-N-**P**-**M**-**SH**-**G**-**F**-**M2**-1/**M2**-2-L-5'. The **G** and **F** glycoproteins are the major **RSV** neutralization and protective antigens. It seems likely that a high level of expression of **G** and **F** would be desirable for a live **RSV** vaccine. For mononegaviruses, the gene order is a major factor controlling the level of mRNA and protein expression due to the polar gradient of sequential transcription. In order to increase the expression of **G** and **F**, recombinant **RSVs** based on strain A2 were constructed in which the **G** or **F** gene was shifted from the sixth or seventh position (in a genome lacking the **SH** gene), resp., to the first position (rRSV-G1/.DELTA. **SH** and rRSV-F1/.DELTA.**SH**, resp.). Another virus was made in which **G** and **F** were shifted together to the

first and second positions, resp. (rRSV-G1F2/.DELTA.**SH**). Shifting one or two genes to the promoter-proximal position resulted in increased mRNA and protein expression of the shifted genes, with **G** and **F** expression increased up to 2.4-and 7.8-fold, resp., at the mRNA level and approx. 2.5-fold at the protein level, compared to the parental virus. Interestingly, the transcription of downstream genes was not greatly affected even though shifting **G** or **F**, or **G** and **F** together, had the consequence of moving the block of genes **NS1-NS2**-N-**P**-**M**-(**G**) one or two positions further from the promoter. The efficiency of replication of the gene shift viruses in vitro was increased up to 10-fold. However, their efficiency of replication in the lower respiratory tracts of mice was statistically indistinguishable from that of the parental virus. In the upper respiratory tract, replication was slightly reduced on some days for viruses in which **G** was in the first position. The magnitude of the **G**-specific antibody response to the gene shift viruses was similar to that to the parental virus, whereas the **F**-specific response was increased up to fourfold, although this was not reflected in an increase of the neutralizing activity. Thus, shifting the **G** and **F** genes to the promoter-proximal position increased virus replication in vitro, had little effect on replication in the mouse, and increased the antigen-specific **immunogenicity** of the virus beyond that of parental **RSV**.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:142851 HCAPLUS
DOCUMENT NUMBER: 136:215388
TITLE: **Immunogenic** hepatitis B nucleocapsid protein (HBc) chimeric particles having enhanced stability
INVENTOR(S): Birkett, Ashley J.
PATENT ASSIGNEE(S): Apovia, Inc., USA
SOURCE: PCT Int. Appl., 290 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014478	A2	20020221	WO 2001-US41759	20010816
WO 2002014478	A3	20030605		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003138769	A1	20030724	US 2001-930915	20010815
AU 2001085452	A5	20020225	AU 2001-85452	20010816
EP 1333857	A2	20030813	EP 2001-964615	20010816
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-225843P P 20000816
US 2000-226867P P 20000822
US 2001-930915 A 20010815

WO 2001-US41759 W 20010816

AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (core protein or HBc) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an **immunogenic** epitope. The **immunogenic** epitope is a B cell epitope or T cell epitope derived from pathogen such as Streptococcus pneumonia, Cryptosporidium parvum, HIV, foot and mouth disease virus, influenza virus, Yersinia pestia, etc. The display of the **immunogenic** epitope is displayed in the **immunogenic** loop of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer mol. Methods of making and using the chimers are also disclosed.

L4 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:31493 HCAPLUS
DOCUMENT NUMBER: 136:101087
TITLE: Attenuated human-bovine chimeric parainfluenza virus (PIV) vaccines
INVENTOR(S): Skiadopoulos, Mario H.; Collins, Peter L.; Murphy, Brian R.; Schmidt, Alexander C.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002605	A2	20020110	WO 2001-US21527	20010705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001071909	A5	20020114	AU 2001-71909	20010705
US 2003082209	A1	20030501	US 2001-900112	20010705
PRIORITY APPLN. INFO.:			US 2000-215809P P	20000705
			WO 2001-US21527 W	20010705

AB Chimeric human-bovine parainfluenza viruses (PIVs) are infectious and attenuated in humans and other mammals and useful individually or in combination in vaccine formulations for eliciting an anti-PIV immune response. Also provided are isolated polynucleotide mols. and vectors incorporating a chimeric PIV genome or antigenome which includes a partial or complete human or bovine PIV "background" genome or antigenome combined or integrated with one or more heterologous gene(s) or genome segment(s) of a different PIV. Chimeric human-bovine PIV of the invention include a partial or complete "background" PIV genome or antigenome derived from or patterned after a human or bovine PIV virus combined with one or more heterologous gene(s) or genome segment(s) of a different PIV virus to form the human-bovine chimeric PIV genome or antigenome. In certain aspects of the invention, chimeric PIV incorporate a partial or complete human PIV

background genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) from a bovine PIV, whereby the resultant chimeric virus is attenuated by virtue of host-range restriction. In alternate embodiments, human-bovine chimeric PIV incorporate a partial or complete bovine PIV background genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) from a human PIV gene that encode a human PIV **immunogenic** protein, protein domain or epitope, for example encoded by PIV HN and/or **F** glycoprotein gene(s) or genome segment(s). Human-bovine chimeric PIV of the invention are also useful as vectors for developing vaccines against other pathogens. A variety of addnl. mutations and nucleotide modifications are provided within the human-bovine chimeric PIV of the invention to yield desired phenotypic and structural effects.

L4 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:283263 HCAPLUS
DOCUMENT NUMBER: 135:59874
TITLE: Chimeric Subgroup A **Respiratory Syncytial Virus** with the Glycoproteins Substituted by Those of Subgroup B and **RSV** without the **M2**-2 Gene Are Attenuated in African Green Monkeys
AUTHOR(S): Cheng, Xing; Zhou, Helen; Tang, Roderick S.; Munoz, Mary G.; Jin, Hong
CORPORATE SOURCE: Aviron, Mountain View, CA, 94043, USA
SOURCE: Virology (2001), 283(1), 59-68
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using the existing reverse genetics system developed for the subgroup A **respiratory syncytial virus** (**RSV**), a chimeric virus (designated rA-GBFB) that expresses subgroup B-specific antigens was constructed by replacing the **G** and **F** genes of the A2 strain with those of the 9320 strain of subgroup B **RSV**. RA-GBFB grew well in tissue culture, but it was attenuated in the respiratory tracts of cotton rats and African green monkeys. To further attenuate this chimeric **RSV**, the **M2**-2 open reading frame was removed from rA-GBFB. RA-GBFB.DELTA.**M2**-2 was highly attenuated in replication in the respiratory tracts of the infected monkeys, but it provided complete protection against wild-type subgroup B **RSV** challenge following two doses of infection. In this study, rA2.DELTA.**M2**-2 (a recombinant A2 **RSV** that lacks the **M2**-2 gene) was also evaluated in African green monkeys. The replication of rA2.DELTA.**M2**-2 was highly restricted in both the upper and lower respiratory tracts of the infected monkeys and it induced titers of serum anti-**RSV** neutralizing antibody that were slightly lower than those induced by wild-type rA2. When rA2.DELTA.**M2**-2-infected monkeys were challenged with wild-type A2 virus, the replication of the challenge virus was reduced by approx. 100-fold in the upper respiratory tract and 45,000-fold in the lower respiratory tracts. RA2.DELTA.**M2**-2 and rA-GBFB.DELTA.**M2**-2 could represent a bivalent **RSV** vaccine compn. for protection against multiple strains from the two **RSV** subgroups. (c) 2001 Academic Press.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:228735 HCAPLUS
DOCUMENT NUMBER: 134:271226

TITLE: Use of an outer membrane protein A of an enterobacterium associated with a **respiratory syncytial virus immunogenic** peptide for preparing vaccines for intranasal administration
INVENTOR(S): Corvaiea, Nathalie; Goestch, Liliane
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021203	A1	20010329	WO 2000-FR2626	20000922
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2798857	A1	20010330	FR 1999-11888	19990923
FR 2798857	B1	20030606		
BR 2000014246	A	20020521	BR 2000-14246	20000922
EP 1218029	A1	20020703	EP 2000-964347	20000922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.: FR 1999-11888 A 19990923
WO 2000-FR2626 W 20000922

AB The invention concerns the use of an outer membrane protein A (OmpA) of an enterobacterium, in particular protein P40 of Klebsiella pneumoniae, assocd. with an **immunogenic** peptide derived from the **respiratory syncytial virus** (**RSV**) for prepg. a pharmaceutical compn. for intranasal administration designed to induce an immune response protecting the upper and lower (lungs) respiratory route against **RSV** infection. The invention also concerns the use of said compds. for prepg. a vaccine for preventing and treating **RSV** infection.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:50779 HCAPLUS
DOCUMENT NUMBER: 134:114850
TITLE: Production of recombinant **respiratory syncytial viruses** expressing immune modulatory molecules
INVENTOR(S): Collins, Peter L.; Bukreyev, Alexander; Murphy, Brian R.; Whitehead, Stephen S.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004271	A2	20010118	WO 2000-US19042	20000712
WO 2001004271	A3	20010719		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000062112	A5	20010130	AU 2000-62112	20000712
EP 1194581	A2	20020410	EP 2000-948641	20000712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000013202	A	20020924	BR 2000-13202	20000712
JP 2003512817	T2	20030408	JP 2001-509475	20000712
PRIORITY APPLN. INFO.:			US 1999-143425P P	19990713
			WO 2000-US19042 W	20000712

AB Recombinant **respiratory syncytial virus** (**RSV**) are provided which express one or more immune modulatory mols. The recombinant virus is modified by addn. or substitution of a sequences encoding the immune modulatory mol. (e.**g.**, cytokines). Introduction of a cytokine increases, decreases, or otherwise enhances aspects of viral biol. and/or host immune responses to **RSV**. In one example, the murine interferon-.gamma. gene was inserted into the **RSV G-F** intergenic region. Cultured cells infected with rRSV/mIFN-.gamma. expressed the cytokine and replication of the recombinant virus was attenuated in upper and lower respiratory tract of infected mice.

L4 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	2000:678573 HCAPLUS
DOCUMENT NUMBER:	133:333659
TITLE:	Recombinant **respiratory syncytial virus** that does not express the **NS1** or **M2**-2 protein is highly attenuated and **immunogenic** in chimpanzees
AUTHOR(S):	Teng, Michael N.; Whitehead, Stephen S.; Bermingham, Alison; St. Claire, Marisa; Elkins, William R.; Murphy, Brian R.; Collins, Peter L.
CORPORATE SOURCE:	Respiratory Viruses Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892, USA
SOURCE:	Journal of Virology (2000), 74(19), 9317-9321 CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Mutant recombinant **respiratory syncytial viruses** (**RSV**) which cannot express the **NS1** and **M2**-2 proteins, designated rA2.DELTA.**NS1** and rA2.DELTA. **M2**-2, resp., were evaluated as live-attenuated **RSV** vaccines. The rA2.DELTA.**NS1** virus contains a large deletion that should have the advantageous property of genetic stability during replication in vitro and in vivo. In vitro, rA2.DELTA.**NS1** replicated approx. 10-fold less well than wild-type recombinant **RSV** (rA2), while rA2.DELTA.**M2**-2 had delayed growth kinetics but reached a final titer similar to that of rA2. Each virus was administered to the respiratory tracts of **RSV**-seroneg. chimpanzees to assess replication, **immunogenicity**, and protective efficacy. The rA2.DELTA.**NS1** and rA2.DELTA.**M2**

-2 viruses were 2,200- to 55,000-fold restricted in replication in the upper and lower respiratory tracts but induced a level of **RSV** -neutralizing antibody in serum that was only slightly reduced compared to the level induced by wild-type **RSV**. The replication of wild-type **RSV** in immunized chimpanzees after challenge was reduced more than 10,000-fold at each site. Importantly, rA2.DELTA. **NS1** and rA2.DELTA.**M2**-2 were 10-fold more restricted in replication in the upper respiratory tract than was the cpts248/404 virus, a vaccine candidate that retained mild reactogenicity in the upper respiratory tracts of 1-mo-old infants. Thus, either rA2.DELTA. **NS1** or rA2.DELTA.**M2**-2 might be appropriately attenuated for this age group, which is the major target population for an **RSV** vaccine. In addn., these results show that neither **NS1** nor **M2**-2 is essential for **RSV** replication in vivo, although each is important for efficient replication.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:775451 HCAPLUS
DOCUMENT NUMBER: 128:60477
TITLE: Recombinant vaccinia viruses expressing the **F** , **G** or N, but not the **M2**, protein of bovine **respiratory syncytial virus** (BRSV) induce resistance to BRSV challenge in the calf and protect against the development of pneumonic lesions
AUTHOR(S): Taylor, Geraldine; Thomas, Lewis H.; Furze, Julie M.; Cook, Roy S.; Wyld, Sara G.; Lerch, Robert; Hardy, Richard; Wertz, Gail W.
CORPORATE SOURCE: Institute for Animal Health, Newbury, RG20 7NN, UK
SOURCE: Journal of General Virology (1997), 78(12), 3195-3206
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **immunogenicity** and protective efficacy of recombinant vaccinia viruses (rVV) encoding the **F**, **G**, N, or **M2** (22K) proteins of bovine **respiratory syncytial virus** (BRSV) were evaluated in calves, the natural host for BRSV. Calves were vaccinated either by scarification or intratracheally with rVV and challenged 6-7 wk later with BRSV. Although replication of rVV expressing the **F** protein in the respiratory tract was limited after intratracheal vaccination, the levels of serum and pulmonary antibody were similar to those induced following scarification. The serum antibody response induced by the **F** protein was biased in favor of IgG1 antibody, whereas the **G** and the N proteins induced similar levels of IgG1:IgG2, and antibody was undetectable in calves primed with the **M2** protein. The **F** protein induced neutralizing antibodies, but only levels of complement-dependent neutralizing antibodies were induced by the **G** protein, and antibody induced by the N protein was not neutralizing. The **F** and N proteins primed calves for BRSV-specific lymphocyte proliferative responses, whereas proliferative responses were detected in calves primed with the **G** protein only after BRSV challenge. The **M2** protein primed lymphocytes in only 1 out of 5 calves. Although there were differences in the immune responses induced by the rVVs, the **F**, **G** and N, but not the **M2**, proteins induced protection against BRSV infection and, in contrast with the enhanced lung pathol. seen in mice vaccinated with rVV expressing individual proteins of human

RSV, there was a redn. in lung pathol. in calves.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:744681 HCAPLUS
DOCUMENT NUMBER: 128:45651
TITLE: Recombinant **respiratory syncytial virus** from which the entire **SH** gene has been deleted grows efficiently in cell culture and exhibits site-specific attenuation in the respiratory tract of the mouse
AUTHOR(S): Bukreyev, Alexander; Whitehead, Stephen S.; Murphy, Brian R.; Collins, Peter L.
CORPORATE SOURCE: Laboratory of Infectious Diseases, National Institute Allergy and Infectious Diseases, Bethesda, MD, 20892-0720, USA
SOURCE: Journal of Virology (1997), 71(12), 8973-8982
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The small hydrophobic protein **SH** of human **respiratory syncytial virus** (**RSV**) is a short transmembrane surface protein of unknown function. A full-length cDNA of **RSV** strain A2 (subgroup A) antigenomic RNA was modified such that the entire **SH** gene, including the transcription signals and the complete mRNA-encoding sequence, was deleted and replaced by a synthetic intergenic region. This reduced the length of the antigenome by 398 nucleotides and ablated expression of 1 of the 10 **RSV** mRNAs. Recombinant virus contg. this engineered deletion was recovered, and the absence of the **SH** gene was confirmed by reverse transcription in conjunction with PCR. Northern blot anal. of intracellular RNAs and gel electrophoresis of labeled intracellular proteins confirmed the lack of expression of the **SH** mRNA and protein. The absence of the **SH** gene did not noticeably affect RNA replication, but two effects on transcription were noted. First, synthesis of the **G**, **F**, and **M2** mRNAs was increased, presumably due to their being one position closer to the promoter in the gene order. Second, transcription of genes downstream of the engineered site exhibited a steeper gradient of polarity. On monolayers of HEp-2 cells, the **SH**-minus virus produced syncytia which were at least equiv. in size to those of the wild type and produced plaques which were 70% larger. Furthermore, the **SH**-minus virus grew somewhat better (up to 12.6-fold) than wild-type recombinant **RSV** in certain cell lines. While the function of the **SH** protein remains to be detd., it seems to be completely dispensable for growth in tissue culture and fusion function. When inoculated intranasally into mice, the **SH**-minus virus resembled the wild-type recombinant virus in its efficiency of replication in the lungs, whereas it replicated 10-fold less efficiently in the upper respiratory tract. In mice, the **SH**-minus and wild-type recombinant viruses were similarly **immunogenic** and effective in inducing resistance to virus challenge.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:739237 HCAPLUS
DOCUMENT NUMBER: 128:33496
TITLE: Structural properties of chimeric peptides containing

a T-cell epitope linked to a fusion peptide and their importance for in vivo induction of cytotoxic T-cell responses

AUTHOR(S): Lelievre, Dominique; Hsu, Shiou-Chih; Daubos, Philippe; Favard, Cyril; Vigny, Paul; Trudelle, Yves; Steward, Michael W.; Delmas, Agnes

CORPORATE SOURCE: Centre de Biophysique Moleculaire, UPR 4301 CNRS, Orleans, F-45071, Fr.

SOURCE: European Journal of Biochemistry (1997), 249(3), 895-904
CODEN: EJBCAI; ISSN: 0014-2956

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have previously shown that when administered to mice without adjuvant, a chimeric peptide consisting of the fusion peptide **F** from measles virus protein linked at the C-terminus of a cytotoxic T-cell epitope from the **M2** protein of **respiratory syncytial virus** efficiently primes for an major histocompatibility complex (MHC) class-I restricted cytotoxic T lymphocyte (CTL) response. Here, the authors demonstrated by microspectrofluorometry that the fusion-peptide moiety bound to the plasma membrane of living cells. When the fusion peptide was linked to the C-terminus of the CTL epitope, the chimeric peptide (**M2-F**) adopted a marked .beta.-sheet conformation. In contrast, when the fusion peptide was linked to the N-terminus of the T-cell epitope (**F-M2**), the chimeric peptide adopted an .alpha.-helical conformation in the presence of trifluoroethanol. The **immunogenicity** of the 2 chimeric peptides for class-I restricted CTL was also different, the one adopting the .alpha.-helical conformation being more **immunogenic**. Probably due to its obvious conversion to an .alpha.-helical conformation, the **F-M2** peptide could have a higher propensity to insert into membranes, as shown by microspectrofluorometry, with a resultant better **immunogenicity** than the **M2-F** peptide.

L4 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:6778 HCAPLUS

DOCUMENT NUMBER: 120:6778

TITLE: Mutant **respiratory syncytial virus** (**RSV**), vaccines containing it, and methods of vaccination with **RSV**

INVENTOR(S): Randolph, Valerie Bruce; Crowley, Joan Coflan

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: Eur. Pat. Appl., 63 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 567100	A1	19931027	EP 1993-106496	19930421
EP 567100	B1	19990317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2094464	AA	19931022	CA 1993-2094464	19930420
ZA 9302763	A	19940208	ZA 1993-2763	19930420
AU 9337057	A1	19931028	AU 1993-37057	19930421
AU 671983	B2	19960919		

JP 06022756	A2	19940201	JP 1993-117812	19930421
AT 177785	E	19990415	AT 1993-106496	19930421
ES 2130189	T3	19990701	ES 1993-106496	19930421

PRIORITY APPLN. INFO.: US 1992-871420 19920421

AB Cold-adapted (attenuated) mutants of **RSV** belonging to subgroup A or B were obtained by repeated passage in Vero cells at .ltoreq.26.degree.. The **immunogenic** peptides are purified and identified, and the nucleic acid segments encoding them are cloned, sequenced, and expressed. The mutants elicited protective immunity against **RSV** challenge in cotton rats and African green monkeys. Monoclonal antibodies to the mutants are useful in diagnostic assays and therapy.

```
=> d que stat 16
L1          4360 SEA FILE=HCAPLUS ABB=ON  (RSV? OR ?RESPIRATOR?(W)?SYNCYTIAL?(W)
                 ?VIRUS?)
L2           187 SEA FILE=HCAPLUS ABB=ON  L1 AND ?IMMUNOGEN?
L3           138 SEA FILE=HCAPLUS ABB=ON  L2 AND (F OR G OR M OR SH OR NS1? OR
                 NS2? OR P)
L4            13 SEA FILE=HCAPLUS ABB=ON  L3 AND M2?
L5            29 SEA L4
L6            19 DUP REMOV L5 (10 DUPLICATES REMOVED)


=>  d ibib abs 16 1-19

L6   ANSWER 1 OF 19  WPIDS  COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER:     2003-559095 [52]   WPIDS
DOC. NO. CPI:         C2003-150701
TITLE:                An immunogenic composition comprising an
                      antigen and a purified M protein from
                      respiratory syncytial virus,
                      useful as a vaccine for immunizing a host or for
                      enhancing the immune response to an antigen in a host.
DERWENT CLASS:        B04 D16
INVENTOR(S):          BARBER, B; CATES, G; PARRINGTON, M; SAMBHARA, S
PATENT ASSIGNEE(S):   (AVET) AVENTIS PASTEUR LTD
COUNTRY COUNT:        102
PATENT INFORMATION:

     PATENT NO   KIND DATE     WEEK      LA   PG
     -------------------------------------------
     WO 2003053464 A1 20030703 (200352)* EN   27
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
            MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
            ZM ZW

APPLICATION DETAILS:

     PATENT NO   KIND                  APPLICATION      DATE
     ------------------------------------------------------------
     WO 2003053464 A1                  WO 2002-CA1953   20021218


PRIORITY APPLN. INFO: US 2001-341422P  20011220
AN   2003-559095 [52]   WPIDS
AB   WO2003053464 A UPAB: 20030813
     NOVELTY - An immunogenic composition comprising an antigen and a
     purified M protein from respiratory syncytial
     virus or at least one of its immunoeffective fragments, is new.
     The M protein or its immunoeffective fragment is provided in a
     pre-selected amount to provide an enhanced immune response to the antigen
     in a host having a pre-existing respiratory syncytial
     virus M-specific immune response.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
     following:
          (1) making an immunogenic composition comprising providing
     an antigen and a purified M protein from respiratory
```

syncytial virus or at least one of its immunoeffective fragment, where the amount of the **M** protein or its immunoeffective fragment is provided in a pre-selected amount to provide an enhanced immune response to the antigen in a host having a pre-existing **respiratory syncytial virus M** -specific immune response;

(2) immunizing a host comprising administering the **immunogenic** composition cited above in a host; and

(3) enhancing an immune response to an antigen in a host having a pre-existing immune response to **respiratory syncytial virus M** protein comprising purifying **M** protein of **respiratory syncytial virus**, mixing a pre-selected amount of the purified **M** protein with a different antigen, formulating the mixture as a vaccine, and administering the vaccine to a host.

ACTIVITY - Virucide.

MECHANISM OF ACTION - Vaccine.

Groups of BALB/c mice were primed with 103 pfu of live **respiratory syncytial virus** (**RSV**) intranasally. Four weeks later, the mice were boosted with phosphate buffered saline, or formalin-inactivated-**RSV** 5 ng of **F** with 1 micro **g** of **M** in aluminum phosphate or 5 ng of **F** in aluminum phosphate. The animals were boosted again four weeks later and the sera samples were collected to determine anti-**F** responses by **F**-specific enzyme-linked immunosorbent assay. The antibody results show that the inclusion of the **RSV M** antigen enhances the antibody response (antibody titer) to **RSV F** antigen by two logs when compared to the **RSV F** only boost.

USE - The **immunogenic** composition is useful as a vaccine for immunizing a host against a disease caused by **respiratory syncytial virus**. The pre-selected amount of purified **M** protein from **respiratory syncytial virus** or its immunoeffective fragment is useful for enhancing the immune response to an antigen in a host having a pre-existing **respiratory syncytial virus M** -specific immune response (claimed).

Dwg.0/4

L6 ANSWER 2 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-381589 [36] WPIDS

DOC. NO. CPI: C2003-101341

TITLE: New **immunogenic** compositions comprising a cocktail of at least four different **RSV** antigens, useful as a vaccine against **respiratory syncytial virus** (**RSV**), which causes respiratory tract infections in infants and children.

DERWENT CLASS: B04 D16

INVENTOR(S): HUANG, S; KUMAR, M; LEONG, K; MOHAPATRA, S S; BEHERA, A K; CHEN, L; LEONG, K W; LOCKEY, R F; MOHAPTRA, S S; PEREZ DE LA CRUZ, C; ZHANG, J

PATENT ASSIGNEE(S): (HUAN-I) HUANG S; (KUMA-I) KUMAR M; (LEON-I) LEONG K; (MOHA-I) MOHAPATRA S S; (UYJO) UNIV JOHNS HOPKINS; (UYSF-N) UNIV SOUTH FLORIDA

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2003028759 A1 20030410 (200336)* EN 35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2003068333 A1 20030410 (200340)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003028759 A1		WO 2002-US4114	20020212
US 2003068333 A1	Provisional	US 2001-325573P	20010928
		US 2002-73065	20020212

PRIORITY APPLN. INFO: US 2001-325573P 20010928; US 2002-73065 20020212
AN 2003-381589 [36] WPIDS
AB WO2003028759 A UPAB: 20030609
NOVELTY - **Immunogenic** compositions for conferring protection in a host against disease caused by **respiratory syncytial virus** (**RSV**) comprising an **F RSV** antigen and a **G RSV** antigen, or an **M2 RSV** antigen; or an **F RSV** antigen, a **G RSV** antigen and an **M2 RSV** antigen, and at least one of **M**, **M2**, **SH**, **NS1**, **NS2**, N, **F**, **G**, or **P RSV** antigen, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a gene expression vaccine for conferring protection in a host against disease caused by **RSV** comprising a plasmid DNA cocktail comprising a combination of at least two **RSV** antigens selected from **F**, **G**, **M**, **M2**, **SH**, **NS1**, **NS2**, N, and **P**; where the plasmid DNA cocktail is coacervated with chitosan to form nanospheres;
(2) immunizing a host against disease caused by infection with **RSV**; and
(3) making a gene expression vaccine.
ACTIVITY - Virucide.
BALB/c mice were orally administered with the composition or naked DNA (25 micro **g** total). Animals were infected with **RSV** on day 16, and 4 days later sacrificed. Results showed that mice given the composition had reduction in epithelial cell damage and interstitial thickening when compared to controls.
MECHANISM OF ACTION - Vaccine.
USE - The composition is useful as a vaccine against **respiratory syncytial virus** (**RSV**), which causes respiratory tract infections in infants and children.
Dwg.0/9

L6 ANSWER 3 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003386614 IN-PROCESS
DOCUMENT NUMBER: 22804932 PubMed ID: 12922094
TITLE: Evaluation of recombinant **respiratory syncytial virus** gene deletion mutants in African green monkeys for their potential as live

attenuated vaccine candidates.
AUTHOR: Jin Hong; Cheng Xing; Traina-Dorge Vicki L; Park Hyun Jung; Zhou Helen; Soike Ken; Kemble George
CORPORATE SOURCE: MedImmune Vaccines Inc., 297 North Bernardo Avenue, 94043, Mountain View, CA, USA.
SOURCE: VACCINE, (2003 Sep 8) 21 (25-26) 3647-52.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030819
Last Updated on STN: 20030819

AB Towards the goal of developing live attenuated **respiratory syncytial virus** (**RSV**) vaccines to prevent severe respiratory tract infections caused by **respiratory syncytial virus**, recombinant **RSV** containing a deletion of single or multiple **NS1**, **NS2**, **SH** and **M2**-2 genes have been generated. In this study, recombinants, rA2DeltaM2-2, rA2DeltaNS2, rA2DeltaNS1NS2, rA2DeltaSHNS2, rA2DeltaM2-2NS2 were evaluated in African green monkeys (AGMs) for their infectivity, **immunogenicity** and protection against wild type (wt) **RSV** challenge. Replication of rA2DeltaNS2 and rA2DeltaSHNS2 was not attenuated in either the upper or the lower respiratory tracts of AGMs. On the other hands, rA2DeltaNS1NS2 was over-attenuated; it did not replicate in the respiratory tracts of the infected monkeys and did not provide sufficient protection against wild type **RSV** challenge. rA2DeltaM2-2NS2 was slightly more attenuated than rA2DeltaM2-2 and provided partial protection against wt **RSV** challenge. rA2DeltaM2-2, and possibly rA2DeltaM2-2NS2, exhibited the attenuated but protective phenotypes in the monkeys that could be further evaluated as potential live attenuated **RSV** vaccine candidates in the clinical studies.

L6 ANSWER 4 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-090518 [12] WPIDS
DOC. NO. CPI: C2002-027998
TITLE: An isolated infectious recombinant **respiratory syncytial virus** (**RSV**) having one or more shifted **RSV** gene(s) or genome segment(s) within the recombinant genome or antigenome, useful as an attenuated vaccine against **RSV** strains.
DERWENT CLASS: B04 D16
INVENTOR(S): BUCHHOLZ, U; COLLINS, P L; KREMPL, C D; MURPHY, B R; WHITEHEAD, S S
PATENT ASSIGNEE(S): (USGO) US GOVERNMENT; (BUCH-I) BUCHHOLZ U; (COLL-I) COLLINS P L; (KREM-I) KREMPL C D; (MURP-I) MURPHY B R; (WHIT-I) WHITEHEAD S S
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002000693	A2	20020103	(200212)*	EN	168

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD

SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001068709 A 20020108 (200235)
US 2002146433 A1 20021010 (200269)
EP 1294858 A2 20030326 (200323) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002000693	A2	WO 2001-US20107	20010622
AU 2001068709	A	AU 2001-68709	20010622
US 2002146433	A1 Provisional	US 2000-213708P	20000623
		US 2001-887469	20010622
EP 1294858	A2	EP 2001-946696	20010622
		WO 2001-US20107	20010622

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001068709	A Based on	WO 200200693
EP 1294858	A2 Based on	WO 200200693

PRIORITY APPLN. INFO: US 2000-213708P 20000623; US 2001-887469 20010622

AN 2002-090518 [12] WPIDS

AB WO 200200693 A UPAB: 20020221

NOVELTY - An isolated infectious recombinant **respiratory syncytial virus** (**RSV**) having one or more shifted **RSV** gene(s) or genome segment(s) within the recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of the **RSV** gene(s) or genome segment(s) within a wild type **RSV** genome or antigenome, is new.

DETAILED DESCRIPTION - An isolated infectious recombinant **respiratory syncytial virus** (**RSV**) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (**P**), a large polymerase protein (L), a RNA polymerase elongation factor, and a partial or complete recombinant **RSV** genome or antigenome having one or more shifted **RSV** gene(s) or genome segment(s) within the recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of the **RSV** gene(s) or genome segment(s) within a wild type **RSV** genome or antigenome.

INDEPENDENT CLAIMS are included for the following:

(1) a method (M1) for stimulating the immune system of an individual to induce protection against **RSV** which comprises administering to the individual an immunologically sufficient amount of the recombinant **RSV** combined with a physiologically acceptable carrier;

(2) an isolated polynucleotide molecule comprising a recombinant **RSV** genome or antigenome having one or more shifted **RSV** gene(s) or genome segment(s) within the recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of the **RSV** gene(s) or genome segment(s) within a wild type **RSV** genome or antigenome;

(3) a method (**M2**) for producing an infectious attenuated recombinant **RSV** particle from one or more isolated

polynucleotide molecules encoding the **RSV**, comprising expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide comprising a recombinant **RSV** genome or antigenome having one or more shifted **RSV** gene(s) or genome segment(s) within the recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-5 distal position relative to a position of the **RSV** gene(s) or genome segment(s) within a wild type **RSV** genome or antigenome, and **RSV** N, **P**, L and RNA polymerase elongation factor proteins;

(4) an isolated infectious chimeric **RSV** comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (**P**), a large polymerase protein (L), a RNA polymerase elongation factor, and a partial or complete bovine **RSV** background genome or antigenome combined with heterologous gene(s) and/or genome segment(s) of a human **RSV** selected from heterologous gene(s) and/or genome segment(s) of **RSV NS1, NS2, M, SH, G**, and/or **F**, to form a human-bovine chimeric **RSV** genome or antigenome; and

(5) an isolated polynucleotide molecule comprising a recombinant **RSV** genome or antigenome comprising a partial or complete bovine **RSV** background genome or antigenome combined with a plurality of heterologous gene(s) and/or genome segment(s) of a human **RSV** selected from heterologous gene(s) and/or genome segment(s) of **RSV NS1, NS2, M, SH, G**, and/or **F** genes, to form a human-bovine chimeric **RSV** genome or antigenome.

ACTIVITY - Antiviral.

No biological data given.

MECHANISM OF ACTION - The recombinant **RSV** elicits an immune response against either human **RSV** A or **RSV** B or both human **RSV** A and **RSV** B (claimed); gene therapy; vaccine.

No biological data given.

USE - The recombinant **RSV** is useful in an attenuated vaccine to elicits an immune response against one or more strains of **RSV**.

Dwg.0/15

L6 ANSWER 5 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-128101 [12] WPIDS

CROSS REFERENCE: 1998-110527 [10]

DOC. NO. NON-CPI: N2003-101703

DOC. NO. CPI: C2003-032723

TITLE: Composition for vaccination, diagnosis and treatment of **respiratory syncytial virus** infection, comprises fusion protein, attachment protein and matrix protein of **respiratory syncytial virus**.

DERWENT CLASS: A96 B04 D16 S03

INVENTOR(S): CATES, G A; KLEIN, M H; OOMEN, R P; SANHUEZA, S E

PATENT ASSIGNEE(S): (CATE-I) CATES G A; (KLEI-I) KLEIN M H; (OOME-I) OOMEN R P; (SANH-I) SANHUEZA S E; (AVET) AVENTIS PASTEUR LTD

COUNTRY COUNT: 101

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002136739	A1	20020926	(200312)*		23
WO 2003022878	A2	20030320	(200330)	EN	

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU

MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002136739 A1	CIP of	US 1996-679060	19960712
	CIP of	WO 1997-CA497	19970711
	CIP of	US 1999-214605	19990503
		US 2001-950655	20010913
WO 2003022878 A2		WO 2002-CA1347	20020903

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2002136739 A1	CIP of	US 6020182
	CIP of	US 6309649

PRIORITY APPLN. INFO: US 2001-950655 20010913; US 1996-679060 19960712; WO 1997-CA497 19970711; US 1999-214605 19990503

AN 2003-128101 [12] WPIDS
CR 1998-110527 [10]
AB US2002136739 A UPAB: 20030513
NOVELTY - A mixture (I) of purified fusion (**F**) protein, attachment (**G**) protein and matrix (**M**) protein of **respiratory syncytial virus** (**RSV**), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) an **immunogenic** composition (II) comprising (I);
(2) producing (M1) a vaccine for protection against **RSV**, by administering (II) to a test host to determine the amount of frequency of administration to confer protection against disease caused by **RSV**, and formulating the **immunogenic** composition in a form suitable for administration to a treated host in accordance with the determined amount and frequency of administration;
(3) producing (**M2**) a coisolated and copurified mixture of proteins of **RSV** (III), by growing **RSV** on cells in a culture medium, separating the grown virus from the culture medium, solubilizing (**F**), (**G**) and (**M**) protein from the separated virus, and coisolating and copurifying the solubilized **RSV** proteins; and
(4) a diagnostic kit (IV) for determining the presence of antibodies in a sample specifically reactive with **F**, **G** or **M** protein of **RSV**, comprising (I), unit for contacting the **immunogenic** composition with the sample to produce complexes comprising **RSV** and any antibodies present in the sample and unit for determining the production of the complexes.

ACTIVITY - Virucide.
MECHANISM OF ACTION - Vaccine.
RSV subunit preparations were used to formulate an alum-adjuvanted vaccine and a placebo control that contained only alum. The total protein present in a single dose of the vaccines of the antigens **RSV F**, **G** and **M** was 100 micro

g, present in 0.5 ml of phosphate buffered saline. In the alum-adjuvanted vaccine, there was 1.5 mg of alum/0.5 ml of vaccine. The vaccines were assessed for stability for 42 months at 5 deg. C, 5 months at 25 deg. C and 5 weeks at 37 deg. C to ensure physical and biological stability over time. Stability studies indicated that the **P** and **G** antigens in the alum-adjuvanted vaccines were stable at 25 deg. C for at least 6 weeks. The vaccine preparations were used to immunize adults, 65 years of age or older. Blood samples were obtained on day 0 (day of immunization), day 32, day 60 and day 180 and **RSV** serology was performed on the serum samples. **RSV** neutralization assay was performed by a plaque reduction method (NA) against **RSV** A and **RSV** B. There was a greater or equal to 2-fold increase in antibody titer or 4-fold increase in antibody titer compared to pre-immunization titers.

USE - (I) is useful as a pharmaceutical substance in a vaccine against disease caused by infection with **respiratory syncytial virus**. (I) and (II) are useful for determining the presence in a sample of antibodies specifically reactive with **F**, **G** or **M** protein of **RSV**, by contacting the sample with (I) to produce complexes comprising **RSV** and any antibodies present in the sample specifically reactive with it, or immunizing a subject with (II) to produce antibodies specific for the proteins and contacting the sample with antibodies to produce complexes, and determining the production of the complexes. (II) is formulated as a vaccine for in vivo administration to a host, especially a primate, human to confer protection against **RSV**. (II) is useful for generating an immune response in a host. (II) is useful for producing monoclonal antibodies specific for (**F**), (**G**) and (**M**) protein of **RSV**, by administering the **immunogenic** composition to at least one mouse to produce at least one immunized mouse, removing B-lymphocytes from the immunized mouse, fusing the B-lymphocytes with myeloma cells, producing hybridomas, cloning the hybridomas which produce a selected anti-**RSV** protein antibody, culturing the selected anti-**RSV** protein antibody-producing clones, and isolating anti-**RSV** protein antibodies from the selected cultures (all claimed).

ADVANTAGE - (I) as a vaccine is safe and highly **immunogenic**.

Dwg.0/6

L6 ANSWER 6 OF 19 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	2002654767 MEDLINE
DOCUMENT NUMBER:	22302303 PubMed ID: 12414935
TITLE:	Recombinant **respiratory syncytial virus** with the **G** and **F** genes shifted to the promoter-proximal positions.
AUTHOR:	Krempl Christine; Murphy Brian R; Collins Peter L
CORPORATE SOURCE:	Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892-8007, USA.
CONTRACT NUMBER:	AI-00087 (NIAID)
SOURCE:	JOURNAL OF VIROLOGY, (2002 Dec) 76 (23) 11931-42. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200212
ENTRY DATE:	Entered STN: 20021105 Last Updated on STN: 20021218

Entered Medline: 20021213

AB The genome of human **respiratory syncytial virus** (**RSV**) encodes 10 mRNAs and 11 proteins in the order 3'-**NS1**-**NS2**-N-**P**-**M**-**SH**-**G**-**F**-**M2**-1/**M2**-2-L-5'. The **G** and **F** glycoproteins are the major **RSV** neutralization and protective antigens. It seems likely that a high level of expression of **G** and **F** would be desirable for a live **RSV** vaccine. For mononegaviruses, the gene order is a major factor controlling the level of mRNA and protein expression due to the polar gradient of sequential transcription. In order to increase the expression of **G** and **F**, recombinant **RSVs** based on strain A2 were constructed in which the **G** or **F** gene was shifted from the sixth or seventh position (in a genome lacking the **SH** gene), respectively, to the first position (rRSV-G1/DeltaSH and rRSV-F1/DeltaSH, respectively). Another virus was made in which **G** and **F** were shifted together to the first and second positions, respectively (rRSV-G1F2/DeltaSH). Shifting one or two genes to the promoter-proximal position resulted in increased mRNA and protein expression of the shifted genes, with **G** and **F** expression increased up to 2.4-and 7.8-fold, respectively, at the mRNA level and approximately 2.5-fold at the protein level, compared to the parental virus. Interestingly, the transcription of downstream genes was not greatly affected even though shifting **G** or **F**, or **G** and **F** together, had the consequence of moving the block of genes **NS1**-**NS2**-N-**P**-**M**-(**G**) one or two positions further from the promoter. The efficiency of replication of the gene shift viruses in vitro was increased up to 10-fold. However, their efficiency of replication in the lower respiratory tracts of mice was statistically indistinguishable from that of the parental virus. In the upper respiratory tract, replication was slightly reduced on some days for viruses in which **G** was in the first position. The magnitude of the **G**-specific antibody response to the gene shift viruses was similar to that to the parental virus, whereas the **F**-specific response was increased up to fourfold, although this was not reflected in an increase of the neutralizing activity. Thus, shifting the **G** and **F** genes to the promoter-proximal position increased virus replication in vitro, had little effect on replication in the mouse, and increased the antigen-specific **immunogenicity** of the virus beyond that of parental **RSV**.

L6 ANSWER 7 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-356173 [37] WPIDS
CROSS REFERENCE: 1999-045317 [04]; 2001-091890 [10]
DOC. NO. CPI: C2001-110518
TITLE: Isolated infectious chimeric parainfluenza virus (PIV), useful in an attenuated vaccine to elicits an immune response against one or more virus(es) selected from human PIV1 (HPIV1), HPIV2 and HPIV3.
DERWENT CLASS: B04 D16 P32
INVENTOR(S): COLLINS, P L; DURBIN, A P; MURPHY, B R; SCHMIDT, A C; SKIADOPOULOS, M H; TAO, T
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (COLL-I) COLLINS P L; (DURB-I) DURBIN A P; (MURP-I) MURPHY B R; (SCHM-I) SCHMIDT A C; (SKIA-I) SKIADOPOULOS M H; (TAOT-I) TAO T
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2001042445 A2 20010614 (200137)* EN 305
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001020731 A 20010618 (200161)
EP 1179054 A2 20020213 (200219) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL RO SI
CN 1347453 A 20020501 (200252)
US 2002155581 A1 20021024 (200273)
JP 2003516148 W 20030513 (200334) 367

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2001042445	A2		WO 2000-US33293	20001208
AU 2001020731	A		AU 2001-20731	20001208
EP 1179054	A2		EP 2000-984052	20001208
			WO 2000-US33293	20001208
CN 1347453	A		CN 2000-805939	20001208
US 2002155581	A1	Provisional	US 1997-47575P	19970523
		Provisional	US 1997-59385P	19970919
		CIP of	US 1998-83793	19980522
		Provisional	US 1999-170195P	19991210
			US 2000-733692	20001208
JP 2003516148	W		WO 2000-US33293	20001208
			JP 2001-544321	20001208

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001020731	A	Based on	WO 200142445
EP 1179054	A2	Based on	WO 200142445
JP 2003516148	W	Based on	WO 200142445

PRIORITY APPLN. INFO: US 1999-459062 19991210; US 1999-170195P 19991210; US 1999-458813 19991210; US 1997-47575P 19970523; US 1997-59385P 19970919; US 1998-83793 19980522; US 2000-733692 20001208

AN 2001-356173 [37] WPIDS
CR 1999-045317 [04]; 2001-091890 [10]
AB WO 200142445 A UPAB: 20030529
NOVELTY - An isolated infectious chimeric parainfluenza virus (PIV), is new.

DETAILED DESCRIPTION - An isolated infectious chimeric parainfluenza virus (PIV), is new.

The virus comprises a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV vector.background genome, or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinants of one or more heterologous pathogen(s) to form a chimeric genome or antigenome.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for stimulating the immune system of an individual to induce protection against PIV, comprising administering an immunologically sufficient amount of the chimeric PIV;

(2) a method for sequential immunization to stimulate the immune system of an individual to induce protection against multiple pathogens comprising administering to a newborn to 4 month old infant an immunologically sufficient amount of a first attenuated chimeric human PIV (HPIV) expressing an antigenic determinant of a non-PIV pathogen and one or more antigenic determinants of HPIV3 and subsequently administering an immunologically sufficient amount of a second attenuated chimeric HPIV expressing an antigenic determinant of a non-PIV pathogen and one or more antigenic determinants of HPIV1 or HPIV2;

(3) an isolated polynucleotide comprising a chimeric PIV genome or antigenome which includes a partial or complete PIV background genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric PIV genome or antigenome;

(4) a method for producing an infectious attenuated chimeric PIV particle from one or more isolated polynucleotide molecules encoding the PIV, comprising expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide comprising a partial or complete PIV vector genome or antigenome of a human or bovine PIV combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric PIV genome or antigenome, and PIV N, **P** and L proteins;

(5) an expression vector comprising an operably linked transcriptional promoter, a polynucleotide sequence which includes a partial or complete PIV vector genome or antigenome of a human or bovine PIV combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric PIV genome or antigenome, and a transcriptional terminator; and

(6) an isolated infectious recombinant PIV comprising a N protein, a **P**, a L, and a PIV genome or antigenome having a polynucleotide insertion of between 150 nucleotides and 4000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), the polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in the recombinant PIV.

ACTIVITY - Antiviral.

Chimpanzees in groups of 4 were inoculated intranasally and intratracbeally with 105 TCID50 of rPIV3-2TM or PIV2/V94 on day 0. NT swab specimens (day 1 to 12) and tracheal lavage (days 2, 4, 6, 8, and 10) samples were collected. Virus titer was determined as previously described (Durbin et al., Virology 261:319-30, 1999), and results are expressed as log10 TCID50/ml. rPIV3-2TM had a lower peak titer than its wild type parent PIV2/V94 and was shed for a significantly shorter duration than PIV2/94, indicating that rPIV3-2TM.is attenuated in chimpanzees. PIV2/94 wild-type virus replicates to low levels in chimpanzees compared to hamsters and AFGs (undefined), while rPIV3-2TM virus was attenuated in each of these model hosts.

MECHANISM OF ACTION - Anti-PIV vaccine.

USE - The chimeric PIV is useful in an attenuated vaccine to elicits an immune response against one or more virus(es) selected from HPIV1, HPIV2 and HPIV3. Preferably, the chimeric PIV elicits an immune response against HPIV3 and another virus selected from HPIV1 or HPIV2. The chimeric PIV may also elicits a polyspecific immune response against HPIV3 and measles or **respiratory syncytial virus**. An immunospecific composition may also contain two chimeric PIVs, where the first chimeric PIV elicits an immune response against HPIV3 and the second

chimeric PIV elicits an immune response against HPIV1 or HPIV2, and where both the first and second chimeric PIVs elicit an immune response against the non-PIV pathogen (all claimed).
Dwg.0/21

L6 ANSWER 8 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-103088 [11] WPIDS
DOC. NO. CPI: C2001-030283
TITLE: Isolated chimeric human-bovine **respiratory syncytial virus** (**RSV**), useful in an attenuated vaccine to elicits an immune response against either or both human **RSV** A or **RSV** B.
DERWENT CLASS: B04 D16
INVENTOR(S): BUCHHOLZ, U; COLLINS, P L; KREMPLE, C D; MURPHI, B R; WHITEHEAD, S S; KREMPL, C D; MURPHY, B R
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004335	A2	20010118	(200111)*	EN	148
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056415	A	20010130	(200127)		
BR 2000013195	A	20020723	(200257)		
EP 1287152	A2	20030305	(200319)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
KR 2002092343	A	20021211	(200328)		
CN 1402792	A	20030312	(200339)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004335	A2	WO 2000-US17755	20000623
AU 2000056415	A	AU 2000-56415	20000623
BR 2000013195	A	BR 2000-13195	20000623
		WO 2000-US17755	20000623
EP 1287152	A2	EP 2000-941756	20000624
		WO 2000-US17755	20000624
KR 2002092343	A	KR 2002-700318	20020109
CN 1402792	A	CN 2000-810119	20000624

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056415	A	Based on	WO 200104335
BR 2000013195	A	Based on	WO 200104335
EP 1287152	A2	Based on	WO 200104335

PRIORITY APPLN. INFO: US 1999-143132P 19990709
AN 2001-103088 [11] WPIDS
AB WO 200104335 A UPAB: 20030214

NOVELTY - An isolated chimeric human-bovine **respiratory syncytial virus** (**RSV**) that is infectious and attenuated in humans, is new.

DETAILED DESCRIPTION - An isolated chimeric human-bovine **respiratory syncytial virus** (**RSV**) that is infectious and attenuated in humans, is new.

The virus comprises a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (**P**), a large polymerase protein (L), a RNA polymerase elongation factor, and a partial or complete **RSV** background genome, or antigenome of a human **RSV** or bovine **RSV**, combined with one or more heterologous gene(s) or genome segment(s) of a different **RSV** to form a human-bovine chimeric **RSV** genome or antigenome.

INDEPENDENT CLAIMS are also included for the following:

(1) a method (M1) for stimulating the immune system of an individual to induce protection against **RSV**, comprising administering an immunologically sufficient amount of the chimeric **RSV**;

(2) an isolated polynucleotide comprising a chimeric **RSV** genome or antigenome which includes a partial or complete **RSV** background genome or antigenome of a human or bovine **RSV** combined with one or more heterologous gene(s) or genome segment(s) of a different **RSV** to form a human-bovine chimeric **RSV** genome or antigenome; and

(3) a method (**M2**) for producing an infectious attenuated chimeric **RSV** particle from one or more isolated polynucleotide molecules encoding the **RSV**, comprising expressing **RSV** N, **P**, L and RNA polymerase elongation factor proteins, and an expression vector comprising the polynucleotide of (2) in a cell or cell-free lysate.

ACTIVITY - Antiviral.

Young chimpanzees which were determined to be seronegative for human **RSV** were inoculated by both the intranasal and intratracheal routes with a dose of 107 pfu (plaque forming units) per ml of rBRSV or rBRSV/A2 at each site. Each virus was administered to two chimpanzees. Following inoculation of the virus, nasopharyngeal swab samples were taken daily on days 1-10 and 12, and tracheal lavage samples were taken on days 2, 5, 6, 8 and 12. Specimens were frozen and **RSV** titers were measured later by plaque assay on HEp-2 cells. The amount of rhinorrhea, a measure of upper respiratory tract illness, was estimated daily and assigned a score of 0-4 (0=none, 1= trace, 2= mild, 3= moderate, 4= severe). The results were compared to historic controls of animals which had received:

(i) 104 pfu of recombinant human **RSV** strain A2 wild type virus per site (Whitehead, et al., J. Virol. 72:4467-4471, 1998) or

(ii) 105 pfu of the live-attenuated rA2cp28/404 strain A2 vaccine candidate per site (Whitehead, et al., J. Virol. 73:343 8-3442, 1999), administered by the same routes.

Wild type human **RSV** was highly permissive in seronegative chimpanzees, and in this exercise replicated to peak mean titers of more than 4.5 log10 pfu per mI of nasal swab or tracheal lavage sample. The peak rhinorrhea score was 2.5. The live- attenuated vaccine candidate rA2cp248/404 (see, e.g., U.S. Patent No. 5,993,824, issued November 30, 1999; International Publication No. WO 98102530; Collins, et al., Proc Natl. Acad. Sci. USA 92:11563-11567,1995; Whitehead, et al., Virology 247:232-239, 1998) replicated to mean peak titers of 2.5 and 1.4 log10 pfu per mI of swab/lavage in the upper and lower respiratory tracts, respectively, and had a peak rhinorrhea score of 0.8. In contrast, there was no detectable replication of recombinant bovine (rBRSV) in either the upper or lower respiratory tracts and no evidence of disease. Thus, even when administered at 100-1000 times the dose of human **RSV**, rBRSV

was highly restricted for replication in chimpanzees. The rBRSV/A2 chimera exhibited replication over several days in both the upper and lower respiratory tract.

The shedding was not detected until day 3 or 5 indicates that it was not carryover from the inoculation, as does the length of time over which virus was recovered. The titers were much lower than observed for wild type human **RSV** and moderately lower than observed for the rA2cp248/404 vaccine candidate. These results indicate that the chimeric virus was highly attenuated. Thus, replacement of the **G** and **F** glycoprotein genes of rBRSV with their human **RSV** counterparts, which transferred the major antigenic determinants, confers improved growth in chimpanzees while other bovine **RSV** genes contribute to a highly attenuated phenotype.

MECHANISM OF ACTION - Immunostimulant; Anti-**RSV** vaccine.

USE - The chimeric **RSV** is useful in an attenuated vaccine to elicits an immune response against either or both human **RSV** A or **RSV** B (claimed).

Dwg.0/13

L6 ANSWER 9 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-103086 [11] WPIDS
DOC. NO. CPI: C2001-030281
TITLE: Isolated infectious recombinant **respiratory syncytial virus** (**RSV**) has a modified genome and is used as a noninfectious subunit vaccine and for the production of viral proteins in cell culture.
DERWENT CLASS: B04 D16
INVENTOR(S): BERMINGHAM, A; COLLINS, P L; MURPHY, B R
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004321	A1	20010118	(200111)*	EN	124

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000059181 A 20010130 (200127)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004321	A1	WO 2000-US18534	20000707
AU 2000059181	A	AU 2000-59181	20000707

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000059181	A	Based on	WO 200104321

PRIORITY APPLN. INFO: US 1999-143097P 19990709
AN 2001-103086 [11] WPIDS
AB WO 200104321 A UPAB: 20010224

NOVELTY - Isolated infectious recombinant **respiratory syncytial virus** (**RSV**) (I) comprises an **RSV** genome or antigenome, major nucleocapsid (N) protein, nucleocapsid phosphoprotein (**P**), large polymerase protein (L) and RNA polymerase elongation factor and has a modification in the genome/antigenome of the second translational open reading frame encoded by the **M2** gene (**M2** ORF2).

DETAILED DESCRIPTION - Isolated infectious recombinant **respiratory syncytial virus** (**RSV**) (I) comprises an **RSV** genome or antigenome, major nucleocapsid (N) protein, nucleocapsid phosphoprotein (**P**), large polymerase protein (L) and RNA polymerase elongation factor and has a modification in the genome/antigenome which is complete or partial deletion of the second translational open reading frame encoded by the **M2** gene (**M2** ORF2) or at least one nucleotide change to reduce/ablate **M2** ORF2 expression.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide molecule (II) comprising a **RSV** genome or antigenome modified by a partial or complete deletion of **M2** ORF2 or one or more nucleotide changes that reduce or ablate expression of **M2** ORF;

(2) a method for producing an infectious attenuated **RSV** particle from one or more isolated polynucleotide molecules encoding the **RSV**;

(3) an isolated infectious recombinant **RSV** (III) comprising an **RSV** genome or antigenome, major nucleocapsid (N) protein, nucleocapsid phosphoprotein (**P**), large polymerase protein (L) and RNA polymerase elongation factor and an amino acid substitution at Asn43 of the **RSV** polymerase gene L; and

(4) a method for producing one or more purified **RSV** proteins comprising infecting a host cell permissive of **RSV** infection with a recombinant **RSV** that has an **M2** ORF deletion or knock-out mutation in its genome or antigenome, isolating the recombinant **RSV** from the host cell and purifying the one or more **RSV** proteins.

ACTIVITY - Immunostimulant; respiratory general; antiinflammatory.

MECHANISM OF ACTION - Vaccine; gene therapy.

Recombinant **RSV** unable to express NS 1 (rA2 Delta **NS1**) or **M2**-2 (rA2 Delta **M2**-2) viruses were administered individually to juvenile **RSV**-seronegative chimpanzees by combined intranasal and intratracheal inoculation at 105 pfu per ml per site. Nasopharyngeal swabs and tracheal lavage samples were collected at intervals over 10 days post infection and assayed for virus titer to monitor virus replication. The mean peak titer for the nasopharyngeal swab was 5 for wild type **RSV**, 1.6 for rA2 Delta **NS1** and 1.5 for rA2 Delta **M2**-2, for the tracheal lavage the mean peak titer was 5.5 for wild type **RSV**, 1.2 for rA2 Delta **NS1** and less than 0.7 for rA2 Delta **M2**-2. The chimpanzees were monitored daily for rhinorrhea, a symptom of upper respiratory tract illness and the mean peak score determined for each group. For the wild type **RSV** the score was 3 (moderate), for rA2 Delta **NS1** it was 2 (mild) and for rA2 Delta **M2**-2 it was 1.8.

USE - (I) elicits a protective immune response to **RSV** in a vaccinated host (claimed). This immune response is protective against serious lower respiratory tract disease e.**g**. pneumonia and bronchioloitis when the individual is subsequently infected with wild type **RSV**. (I) is administered to an individual seronegative for antibodies to **RSV** or possessing transplacentally acquired maternal antibodies to **RSV**. (I) elicits an immune response

against human **RSV** A and/or **RSV** B (claimed). (I) can be used for the production of viral proteins in cell culture.

The **M2** ORF2 deletion or knockout mutant is also used as a vector for transient gene therapy of the respiratory tract. The vector incorporates a sequence encoding a product of interest e.**g**. cytokines such as interleukin 2 (IL-2), IL-4, interferon gamma (IF-gamma) and granulocyte-macrophage colony stimulating factor (GM-CSF).

ADVANTAGE - Previously a chemotherapeutic agent ribavirin and pooled donor IgG has been used to treat human **RSV** but these methods lack long-term effectiveness and are inappropriate for widespread use.

Dwg.0/6

L6 ANSWER 10 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2001-081053 [09] WPIDS
DOC. NO. CPI: C2001-023408
TITLE: Isolated human-bovine chimeric parainfluenza virus (PIV), useful in an attenuated vaccine to elicits an immune response against one or more virus(es) selected from human PIV1 (HPIV1), HPIV2 and HPIV3.
DERWENT CLASS: B04 D16
INVENTOR(S): BAILLY, J E; COLLINS, P L; DURBIN, A P; MURPHY, B R; SCHMIDT, A C; SKIADOPOULOS, M H
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004320	A1	20010118	(200109)*	EN	148
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056303	A	20010130	(200127)		
EP 1194564	A1	20020410	(200232)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000013190	A	20020716	(200255)		
KR 2002022768	A	20020327	(200264)		
CN 1369011	A	20020911	(200282)		
JP 2003504064	W	20030204	(200320)		170

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004320	A1	WO 2000-US17066	20000616
AU 2000056303	A	AU 2000-56303	20000616
EP 1194564	A1	EP 2000-941614	20000616
		WO 2000-US17066	20000616
BR 2000013190	A	BR 2000-13190	20000615
		WO 2000-US17066	20000615
KR 2002022768	A	KR 2002-700325	20020109
CN 1369011	A	CN 2000-810120	20000616
JP 2003504064	W	WO 2000-US17066	20000616
		JP 2001-509524	20000616

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056303	A	Based on	WO 200104320
EP 1194564	A1	Based on	WO 200104320
BR 2000013190	A	Based on	WO 200104320
JP 2003504064	W	Based on	WO 200104320

PRIORITY APPLN. INFO: US 1999-143134P 19990709
AN 2001-081053 [09] WPIDS
AB WO 200104320 A UPAB: 20021105
NOVELTY - An isolated human-bovine chimeric parainfluenza virus (PIV) that is infectious and attenuated in humans, is new.

DETAILED DESCRIPTION - An isolated human-bovine chimeric parainfluenza virus (PIV) that is infectious and attenuated in humans, is new.

The virus comprises a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (**P**), a large polymerase protein (L), and a partial or complete PIV background genome, or antigenome of a human PIV (HPIV) or bovine PIV (BPIV), combined with one or more heterologous gene(s) or genome segment(s) of a different PIV to form a human-bovine chimeric PIV genome or antigenome.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for stimulating the immune system of an individual to induce protection against PIV, comprising administering an immunologically sufficient amount of the chimeric PIV;

(2) an isolated polynucleotide comprising a chimeric PIV genome or antigenome which includes a partial or complete PIV background genome or antigenome of a human or bovine PIV combined with a heterologous gene or genome segment of a different PIV to form a human-bovine chimeric PIV genome or antigenome;

(3) a method for producing an infectious attenuated chimeric PIV particle from one or more isolated polynucleotide molecules encoding the PIV, comprising expressing PIV N, **P**, and L proteins, and an expression vector comprising the polynucleotide of (2) in a cell or cell-free lysate; and

(4) an expression vector comprising an operably linked transcriptional promoter, the polynucleotide sequence of (2) and a transcriptional terminator.

ACTIVITY - Antiviral.

The rJS (wild-type HPIV3), Ka parent (Kansas BPIV3 strain), cKa (chimeric Ka strain), SF parent (Shipping fever BPIV3 strain) and cSF (chimeric SF strain) were administered intranasally and intratracheally at a dose of 100000 TCID50 per site to rhesus monkeys. Replication was monitored using standard procedures for obtaining samples from the upper (nasopharyngeal swab specimens) and lower (tracheal lavage specimens) respiratory tract and for titering the virus in LLC-MK2 cells. The cKa and cSF recombinants were significantly attenuated for the upper respiratory tract exhibiting, respectively, a 63-fold or a 32-fold reduction in mean peak virus titer compared to that of the rJS HPIV3 parent. Both cKa and cSF were also attenuated for the lower respiratory tract, but this difference was only statistically significant for cSF. The low level of replication of rJS in the lower respiratory tract made it difficult to demonstrate in a statistically-significant fashion further restriction of replication due to an attenuation phenotype at this site.

The level of replication of each chimeric virus, cKa and cSF, was not significantly different from its bovine parent in the upper or the lower respiratory tract, although the chimeric viruses each replicated better than their BPIV3 parents in the upper respiratory tract.

MECHANISM OF ACTION - Anti-PIV vaccine.

USE - The chimeric PIV is useful in an attenuated vaccine to elicits an immune response against one or more virus(es) selected from HPIV1, HPIV2 and HPIV3.

Preferably, the chimeric PIV elicits an immune response against HPIV3 and another virus selected from HPIV1, HPIV2 or HPIV3 (claimed).

Dwg.0/11

L6 ANSWER 11 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-091926 [10] WPIDS
DOC. NO. CPI: C2001-027208
TITLE: Recombinant **respiratory syncytial virus** (**RSV**) incorporating a heterologous polynucleotide encoding an immune modulatory molecule is used as a vaccine to provide an immune response to **RSV**.
DERWENT CLASS: B04 D16
INVENTOR(S): BURKREYEV, A; COLLINS, P L; MURPHY, B R; WHITEHEAD, S S; BUKREYEV, A
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004271	A2	20010118	(200110)*	EN	154
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000062112	A	20010130	(200127)		
EP 1194581	A2	20020410	(200232)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000013202	A	20020924	(200272)		
CN 1384883	A	20021211	(200324)		
KR 2002092889	A	20021212	(200328)		
JP 2003512817	W	20030408	(200333)		180

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004271	A2	WO 2000-US19042	20000712
AU 2000062112	A	AU 2000-62112	20000712
EP 1194581	A2	EP 2000-948641	20000712
		WO 2000-US19042	20000712
BR 2000013202	A	BR 2000-13202	20000712
		WO 2000-US19042	20000712
CN 1384883	A	CN 2000-810303	20000712
KR 2002092889	A	KR 2002-700505	20020114
JP 2003512817	W	WO 2000-US19042	20000712
		JP 2001-509475	20000712

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000062112	A	Based on	WO 200104271

EP 1194581 A2 Based on WO 200104271
BR 2000013202 A Based on WO 200104271
JP 2003512817 W Based on WO 200104271

PRIORITY APPLN. INFO: US 1999-143425P 19990713
AN 2001-091926 [10] WPIDS
AB WO 200104271 A UPAB: 20010220
NOVELTY - Infectious recombinant **respiratory syncytial virus** (**RSV**) (I) comprising a recombinant **RSV** genome or antigenome incorporating a heterologous polynucleotide encoding an immune modulatory molecule, a major nucleocapsid (N) protein, nucleocapsid phosphoprotein (**P**), large polymerase protein (L) and a RNA polymerase elongation factor, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide molecule (II) comprising a **RSV** genome or antigenome modified to incorporate a polynucleotide sequence encoding an immune modulatory molecule; and

(2) a method for producing an infectious attenuated **RSV** particle from one or more isolated polynucleotide molecules encoding the **RSV**.

ACTIVITY - Immunostimulator.

Balb/c mice were infected intranasally with 106 plaque forming units (pfu) rRSV/mIFN gamma , rRSV/chloramphenicol acetyl transferase (CAT) or wt **RSV**. Serum samples were collected on days 0, 28 and 56 and analyzed by **RSV**-specific and antibody isotype-specific enzyme linked immunosorbent assay and by an **RSV** neutralization assay. The levels of IgA antibodies induced by the viruses were not significantly different, there was a significant increase, four fold, in total IgG specific to **RSV F** protein in mice vaccinated with rRSV/mIFN gamma compared to animals vaccinated with wt **RSV** or **RSV**/CAT on day 56 but not on day 28. Neutralizing antibody titers of mice infected with rRSV/mIFN gamma compared with wt **RSV** and **RSV**/CAT were lower on day 28 but modestly higher on day 56.

MECHANISM OF ACTION - Vaccine.

USE - (I) elicits a protective immune response to **RSV** in a vaccinated host (claimed). (I) is administered to an individual seronegative for antibodies to **RSV** or possessing transplacentally acquired maternal antibodies to **RSV**. (I) elicits an immune response against human **RSV** A and/or **RSV** B.

ADVANTAGE - (I) induces titers of serum Immunoglobulin **G** (IgG) that are at least 2-10 fold higher than levels of serum IgG induced by wt **RSV**.

Previously a chemotherapeutic agent ribavirin and pooled donor IgG has been used to treat **RSV** but these methods lack long-term effectiveness and are inappropriate for widespread use.

Dwg.0/7

L6 ANSWER 12 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-071448 [08] WPIDS
CROSS REFERENCE: 2002-520377 [56]
DOC. NO. CPI: C2001-020057
TITLE: Obtaining an attenuated vaccine comprising recombining nucleic acids that comprise a complete or partial genomic library of a virus or cell and screening to identify those that are attenuated, useful for treating viral infections.
DERWENT CLASS: B04 D16
INVENTOR(S): APT, D; DELCARDAYRE, S; HOWARD, R; PUNNONEN, J; STEMMER,

W P C
PATENT ASSIGNEE(S): (MAXY-N) MAXYGEN INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001000234	A2	20010104	(200108)*	EN	117
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000058809	A	20010131	(200124)		
EP 1196552	A2	20020417	(200233)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003503039	W	20030128	(200309)		149

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001000234	A2	WO 2000-US16984	20000620
AU 2000058809	A	AU 2000-58809	20000620
EP 1196552	A2	EP 2000-944760	20000620
		WO 2000-US16984	20000620
JP 2003503039	W	WO 2000-US16984	20000620
		JP 2001-505941	20000620

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000058809	A	Based on	WO 200100234
EP 1196552	A2	Based on	WO 200100234
JP 2003503039	W	Based on	WO 200100234

PRIORITY APPLN. INFO: US 1999-344655 19990625
AN 2001-071448 [08] WPIDS
CR 2002-520377 [56]
AB WO 200100234 A UPAB: 20030206
NOVELTY - A method (M1) for obtaining an attenuated vaccine comprising recombining first nucleic acids that comprise a complete or partial genomic library of a virus or cell with a second set and screening to identify those that are attenuated, is new.

DETAILED DESCRIPTION - A method (M1) of obtaining an attenuated vaccine comprises:

(a) recombining a first set of nucleic acid segments that comprises a complete or partial genomic library of a cell with a second set of nucleic acid segments to form a library of recombinant nucleic acid fragments;

(b) screening viruses or cells that contain members of the library of recombinant nucleic acid fragments to identify those viruses or cells that are attenuated under physiological conditions that exist in a host organism; and

(c) screening the attenuated viruses or cells to identify those that can induce an immune response against a pathogenic agent that displays an **immunogenic** determinant that is also displayed by the attenuated viruses or cells.

INDEPENDENT CLAIMS are also included for the following:
(1) an attenuated virus or cell obtained by M1;
(2) a vaccine composition comprising the virus or cell of (1);
(3) a method (**M2**) for vaccinating an animal comprising administering the composition of (2);
(4) a method (M3) for obtaining a chimeric attenuated vaccine comprising:
(a) recombining a first set of one or more nucleic acid segments from a virus or cell with a second set of one or more nucleic acid segments, where the nucleic acid segments of the second set confer upon viruses or cells that contain the nucleic acid segments a property that is desirable for vaccination, to form a library of recombinant DNA fragments;
(b) identifying attenuated viruses or cells by screening viruses or cells that contain members of the library of recombinant DNA fragments to identify those viruses or cells that are attenuated under physiological conditions present in a host organism inoculated with the viruses or cells; and
(c) screening the attenuated viruses or cells to identify those that exhibit an improvement in the property that is desirable for vaccination;
(5) a chimeric attenuated vaccine that comprises an attenuated virus or cell obtained by M3;
(6) a vaccine composition comprising an attenuated virus or cell of (5); and
(7) a method (M4) of vaccinating an animal comprising administering the composition of (6).
ACTIVITY - Antiviral; antibacterial; antiparasitic.
No biological data is given.
MECHANISM OF ACTION - Vaccine.
No biological data is given.
USE - The methods are useful for producing engineered attenuated vaccines which can be used against pathogenic agents such as viruses, bacteria, and parasites.
ADVANTAGE - The vaccines have improved expression of an **immunogenic** polypeptide, improved specific uptake, enhanced stability and enhanced **immunogenecity**.
Dwg.0/6

L6 ANSWER 13 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-687044 [67] WPIDS
DOC. NO. CPI: C2000-208979
TITLE: Producing attenuated negative stranded RNA virus vaccines from cloned sequences, useful for immunizing against e.g. **respiratory syncytial virus**, human parainfluenza virus, Sendai virus Newcastle disease virus, mumps virus and measles virus.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): COLLINS, P L; DURBIN, A P; MURPHY, B R; SKIADOPOULOS, M H
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000061737	A2	20001019	(200067)*	EN	136

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000042315 A 20001114 (200108)
EP 1171623 A2 20020116 (200207) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CN 1347458 A 20020501 (200252)
KR 2002008831 A 20020131 (200254)
BR 2000011159 A 20020723 (200257)
JP 2002541798 W 20021210 (200301) 155

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000061737	A2	WO 2000-US9695	20000412
AU 2000042315	A	AU 2000-42315	20000412
EP 1171623	A2	EP 2000-922075	20000412
		WO 2000-US9695	20000412
CN 1347458	A	CN 2000-806224	20000412
KR 2002008831	A	KR 2001-713102	20011013
BR 2000011159	A	BR 2000-11159	20000412
		WO 2000-US9695	20000412
JP 2002541798	W	JP 2000-611661	20000412
		WO 2000-US9695	20000412

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000042315	A	Based on	WO 200061737
EP 1171623	A2	Based on	WO 200061737
BR 2000011159	A	Based on	WO 200061737
JP 2002541798	W	Based on	WO 200061737

PRIORITY APPLN. INFO: US 1999-129006P 19990413
AN 2000-687044 [67] WPIDS
AB WO 200061737 A UPAB: 20001223
NOVELTY - A method for producing attenuated negative stranded RNA virus vaccines from cloned sequences, is new.

DETAILED DESCRIPTION - A method (I) for producing an isolated, attenuated, recombinant negative stranded RNA virus (nsRV) from 1 or more isolated polynucleotide molecules encoding the nsRV, comprising co-expressing (in a cell or cell-free system) 1 or more expression vectors which comprise 1 or more polynucleotide molecules encoding a recombinant genome or antigenome and essential viral proteins necessary to produce an infective virus particle of the nsRV. The recombinant genome or antigenome is modified to encode a mutation within a recombinant protein of the recombinant virus at an amino acid position corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nsRV. The mutation, by incorporation within the recombinant protein confers an attenuated phenotype on the recombinant virus.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated attenuated recombinant nsRV comprising a recombinant genome or antigenome and essential viral proteins necessary to produce an infectious particle of the recombinant nsRV (the recombinant genome or antigenome is modified to encode a mutation within a recombinant protein of the virus at an amino acid position corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nsRV (the mutation, by incorporation within the recombinant protein confers an attenuated phenotype on the recombinant virus); and

(2) an expression vector comprising an operably linked

transcriptional promoter, a polynucleotide molecule encoding a recombinant genome or antigenome of a recombinant nsRV and a transcriptional terminator (the recombinant genome or antigenome is modified to encode a mutation within a recombinant protein of the virus at an amino acid position corresponding to an amino acid position of an attenuating mutation identified in a heterologous mutant nsRV; the mutation by incorporation within the recombinant protein confers an attenuated phenotype on the recombinant virus).

ACTIVITY - Antiviral.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The recombinant viruses produced may be used for stimulating a patients immune system to induce protection against a negative stranded RNA virus (nsRV) (claimed) such as **respiratory syncytial virus** (**RSV**), especially human **RSV** subgroups A and B, bovine **RSV**, murine **RSV** or avian pneumovirus, human parainfluenza virus (HPIV) 1, HPIV2, HPIV 3, bovine PIV (BPIV), Sendai virus (SeV), Newcastle disease virus (NDV), simian virus 5 (SV5), mumps virus (MuV), measles virus (MeV), canine distemper virus (CDV), rabies virus (RaV) or vesicular stomatitis virus (VSV).

Dwg.0/5

L6 ANSWER 14 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-679462 [66] WPIDS
DOC. NO. CPI: C2000-206611
TITLE: Infectious chimeric **respiratory syncytial virus** (**RSV**) produced from cloned nucleotide sequences, useful as a vaccine against diseases caused by the virus, such as pneumoniae and bronchiolitis.
DERWENT CLASS: B04 D16
INVENTOR(S): COLLINS, P L; MURPHY, B R; WHITEHEAD, S S
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000061611	A2	20001019	(200066)*	EN	278
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000040655	A	20001114	(200108)		
EP 1169457	A2	20020109	(200205)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
KR 2002013526	A	20020220	(200257)		
BR 2000011160	A	20021008	(200277)		
CN 1364195	A	20020814	(200280)		
JP 2002541785	W	20021210	(200301)		309

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000061611	A2	WO 2000-US8802	20000331
AU 2000040655	A	AU 2000-40655	20000331

EP 1169457	A2	EP 2000-920058	20000331
		WO 2000-US8802	20000331
KR 2002013526	A	KR 2001-713099	20011013
BR 2000011160	A	BR 2000-11160	20000331
		WO 2000-US8802	20000331
CN 1364195	A	CN 2000-806217	20000331
JP 2002541785	W	JP 2000-611553	20000331
		WO 2000-US8802	20000331

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000040655	A	Based on	WO 200061611
EP 1169457	A2	Based on	WO 200061611
BR 2000011160	A	Based on	WO 200061611
JP 2002541785	W	Based on	WO 200061611

PRIORITY APPLN. INFO: US 1999-291894 19990413
AN 2000-679462 [66] WPIDS
AB WO 200061611 A UPAB: 20001219
NOVELTY - An isolated infectious chimeric **respiratory syncytial virus** (**RSV**) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (**P**), a large polymerase protein (L), an RNA polymerase elongation factor, and a partial or complete **RSV** genome or antigenome of one **RSV** strain or subgroup virus combined with a heterologous gene of a different **RSV** strain or subgroup virus, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for stimulating the immune system of an individual to induce protection against **RSV** comprising administering the chimeric **RSV**;

(2) an isolated polynucleotide molecule comprising a chimeric **RSV** genome or antigenome which includes a partial or complete **RSV** genome or antigenome of one **RSV** strain or subgroup virus combined with a heterologous gene or gene segment of a different **RSV** strain or subgroup virus; and

(3) a method for producing an infectious attenuated chimeric particle from one or more isolated polynucleotide molecules encoding the **RSV**, comprising expressing in a cell or cell-free lysate, an expression vector comprising an isolated polynucleotide comprising a chimeric **RSV** genome or antigenome and **RSV** N, **P**, L and RNA polymerase elongation factor proteins.

ACTIVITY - Antiviral.
No relevant biological data is given.
MECHANISM OF ACTION - Vaccine.
No relevant biological data is given.
USE - The chimeric **respiratory syncytial virus** (**RSV**) is useful as a vaccine against **RSV** which causes diseases such as pneumoniae and bronchiolitis in infants.
Dwg.0/27

L6 ANSWER 15 OF 19 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000473581 MEDLINE
DOCUMENT NUMBER: 20438131 PubMed ID: 10982380
TITLE: Recombinant **respiratory syncytial virus** that does not express the **NS1** or **M2**-2 protein is highly attenuated and **immunogenic** in chimpanzees.

AUTHOR: Teng M N; Whitehead S S; Bermingham A; St Claire M; Elkins W R; Murphy B R; Collins P L
CORPORATE SOURCE: Respiratory Viruses Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, 20892, USA.
CONTRACT NUMBER: AI-000087 (NIAID)
AI-000099 (NIAID)
SOURCE: JOURNAL OF VIROLOGY, (2000 Oct) 74 (19) 9317-21.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001004

AB Mutant recombinant **respiratory syncytial viruses** (**RSV**) which cannot express the **NS1** and **M2**-2 proteins, designated rA2DeltaNS1 and rA2DeltaM2-2, respectively, were evaluated as live-attenuated **RSV** vaccines. The rA2DeltaNS1 virus contains a large deletion that should have the advantageous property of genetic stability during replication in vitro and in vivo. In vitro, rA2DeltaNS1 replicated approximately 10-fold less well than wild-type recombinant **RSV** (rA2), while rA2DeltaM2-2 had delayed growth kinetics but reached a final titer similar to that of rA2. Each virus was administered to the respiratory tracts of **RSV**-seronegative chimpanzees to assess replication, **immunogenicity**, and protective efficacy. The rA2DeltaNS1 and rA2DeltaM2-2 viruses were 2,200- to 55,000-fold restricted in replication in the upper and lower respiratory tracts but induced a level of **RSV**-neutralizing antibody in serum that was only slightly reduced compared to the level induced by wild-type **RSV**. The replication of wild-type **RSV** in immunized chimpanzees after challenge was reduced more than 10,000-fold at each site. Importantly, rA2DeltaNS1 and rA2DeltaM2-2 were 10-fold more restricted in replication in the upper respiratory tract than was the cpts248/404 virus, a vaccine candidate that retained mild reactogenicity in the upper respiratory tracts of 1-month-old infants. Thus, either rA2DeltaNS1 or rA2DeltaM2-2 might be appropriately attenuated for this age group, which is the major target population for an **RSV** vaccine. In addition, these results show that neither **NS1** nor **M2**-2 is essential for **RSV** replication in vivo, although each is important for efficient replication.

L6 ANSWER 16 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-437001 [37] WPIDS
DOC. NO. CPI: C1998-132762
TITLE: Ester polymers from hydroxy acids and hydroxy amino acids - are biocompatible and biodegradable, as carrier for bioactive materials, e.**g**. vaccines, proteins, anti-sense oligo-nucleotide(s), drugs.
DERWENT CLASS: A23 A96 B04 D16
INVENTOR(S): CHONG, P; KLEIN, M H; SOKOLL, K K
PATENT ASSIGNEE(S): (CONN-N) CONNAUGHT LAB LTD; (AVET) AVENTIS PASTEUR LTD
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9828357	A1	19980702	(199837)*	EN	146

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA
PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW
MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN
YU ZW

AU 9854721 A 19980717 (199848)
EP 946624 A1 19991006 (199946) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6042820 A 20000328 (200023)
JP 2000509428 W 20000725 (200041) 133
BR 9714065 A 20001024 (200058)
MX 9905724 A1 19991001 (200103)
NZ 336718 A 20010126 (200109)
AU 729305 B 20010201 (200112)
US 6228423 B1 20010508 (200128)
US 6287604 B1 20010911 (200154)
US 6312732 B1 20011106 (200170)
JP 3242118 B2 20011225 (200203) 58
JP 2002138139 A 20020514 (200236) 52
US 6471996 B1 20021029 (200274)
EP 946624 B1 20030402 (200325) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69720516 E 20030508 (200338)
JP 3428972 B2 20030722 (200350) 52

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9828357	A1		WO 1997-CA980	19971219
AU 9854721	A		AU 1998-54721	19971219
EP 946624	A1		EP 1997-951024	19971219
			WO 1997-CA980	19971219
US 6042820	A		US 1996-770850	19961220
JP 2000509428	W		WO 1997-CA980	19971219
			JP 1998-528169	19971219
BR 9714065	A		BR 1997-14065	19971219
			WO 1997-CA980	19971219
MX 9905724	A1		MX 1999-5724	19990618
NZ 336718	A		NZ 1997-336718	19971219
			WO 1997-CA980	19971219
AU 729305	B		AU 1998-54721	19971219
US 6228423	B1	Div ex	US 1996-770850	19961220
			US 2000-501373	20000211
US 6287604	B1	Div ex	US 1996-770850	19961220
			US 2000-502674	20000211
US 6312732	B1	Div ex	US 1996-770850	19961220
			US 2000-499533	20000211
JP 3242118	B2		WO 1997-CA980	19971219
			JP 1998-528169	19971219
JP 2002138139	A	Div ex	JP 1998-528169	19971219
			JP 2001-255329	19971219
US 6471996	B1	Div ex	US 1996-770850	19961220
			US 2000-499532	20000211
EP 946624	B1		EP 1997-951024	19971219
			WO 1997-CA980	19971219
DE 69720516	E		DE 1997-620516	19971219
			EP 1997-951024	19971219
			WO 1997-CA980	19971219

JP 3428972	B2	Div ex	JP 1998-528169	19971219
			JP 2001-255329	19971219

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9854721	A	Based on	WO 9828357
EP 946624	A1	Based on	WO 9828357
JP 2000509428	W	Based on	WO 9828357
BR 9714065	A	Based on	WO 9828357
NZ 336718	A	Based on	WO 9828357
AU 729305	B	Previous Publ.	AU 9854721
		Based on	WO 9828357
US 6228423	B1	Div ex	US 6042820
US 6287604	B1	Div ex	US 6042820
US 6312732	B1	Div ex	US 6042820
JP 3242118	B2	Previous Publ.	JP 200009428
		Based on	WO 9828357
US 6471996	B1	Div ex	US 6042820
EP 946624	B1	Based on	WO 9828357
DE 69720516	E	Based on	EP 946624
		Based on	WO 9828357
JP 3428972	B2	Previous Publ.	JP 2002138139

PRIORITY APPLN. INFO: US 1996-770850 19961220; US 2000-501373 20000211; US 2000-502674 20000211; US 2000-499533 20000211; US 2000-499532 20000211

AN 1998-437001 [37] WPIDS

AB WO 9828357 A UPAB: 19980916

Biodegradable, biocompatible ester polymer from hydroxy acids and hydroxy (or thio) amino acids of formula (I) is new. R1-R5 = H or alkyl; R6 = H, a protecting group, a spacer molecule, or a biologically active agent; X = O or S; and x, y are integers. ALso claimed are: (i) Preparation of the polymer comprising: (a) forming a monomer mixture containing at least one alpha -hydroxy acid and at least one pseudo amino acid having an amine protecting group with an organic solvent solution of an esterification catalyst under inert atmospheric conditions; (b) copolymerising the monomers; and (c) isolating the polymer; (ii) a particulate carrier for delivery of biologically active materials to a host comprising a polymer backbone of formula (I); (iii) a composition comprising the particulate carrier in (ii) and at least one biologically active material entrapped within; (iv) preparation of a particulate carrier for delivery of biologically active materials to a host; (v) an **immunogenic** composition comprising the particulate carrier in (ii), an **immunogen** and a physiolgically acceptable carrier.

USE - (I) can be formed into films or microparticles, to serve as particulate carriers for slow or delayed release delivery of biologically active materials for diagnostic or therapeutic purposes. The bioactive materials are mixed into or entrapped within the copolymer, or even coupled to them, optionally through a spacer. Preferred (I) degrade in the body to benign metabolites which occur naturally, to release the bioactive agent. The bioactives are especially vaccines or similar agents which elicit an **immunogenic** response; examples are H, influenzae proteins, including non-proteolytic Hin-47 analogue, D15, P1, P2 and P6; influenza virus or its protein, as multivalent or monovalent influenza virus vaccine; Moraxella catarrhalis protein e.**g**. Tbp2 protein; and Helicobacter pylori protein, e.**g**. urease. Other bioactives are proteins and their mimetics, bacteria and their lysates, viruses, e.**g**. **respiratory syncytial virus**,

virus infected cell lysates, DNA plasmids, antisense RNA, DNA, and oligonucleotides, peptides, e.g. CLTB-36 and **M2**, antigens, antibodies, a wide range of pharmacological agents (e.g. analgesics, antibiotics, antihypertensives, and steroids), carbohydrates, lipids, lipidated amino acids, glycolipids, haptens, or combinations of the above. Attached bioactive agents include cell bioadhesion groups, macrophage stimulators, polyamino acids, and polyethylene glycol. In diagnosis, imaging agents, together with the appropriate antibody to provide targeting, diseased tissue can be monitored or the disease identified. These can be made up as kits. Antibiotic compositions of (I) can also be used as coatings, for surgical implants, catheters, and other devices, to combat infections. Dwg.0/21

L6 ANSWER 17 OF 19 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 1998037604 MEDLINE
DOCUMENT NUMBER: 98037604 PubMed ID: 9371553
TITLE: Recombinant **respiratory syncytial virus** from which the entire **SH** gene has been deleted grows efficiently in cell culture and exhibits site-specific attenuation in the respiratory tract of the mouse.
AUTHOR: Bukreyev A; Whitehead S S; Murphy B R; Collins P L
CORPORATE SOURCE: Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892-0720, USA.
SOURCE: JOURNAL OF VIROLOGY, (1997 Dec) 71 (12) 8973-82. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980116
Last Updated on STN: 19980116
Entered Medline: 19971224

AB The small hydrophobic protein **SH** of human **respiratory syncytial virus** (**RSV**) is a short transmembrane surface protein of unknown function. A full-length cDNA of **RSV** strain A2 (subgroup A) antigenomic RNA was modified such that the entire **SH** gene, including the transcription signals and the complete mRNA-encoding sequence, was deleted and replaced by a synthetic intergenic region. This reduced the length of the antigenome by 398 nucleotides and ablated expression of 1 of the 10 **RSV** mRNAs. Recombinant virus containing this engineered deletion was recovered, and the absence of the **SH** gene was confirmed by reverse transcription in conjunction with PCR. Northern blot analysis of intracellular RNAs and gel electrophoresis of labeled intracellular proteins confirmed the lack of expression of the **SH** mRNA and protein. The absence of the **SH** gene did not noticeably affect RNA replication, but two effects on transcription were noted. First, synthesis of the **G**, **F**, and **M2** mRNAs was increased, presumably due to their being one position closer to the promoter in the gene order. Second, transcription of genes downstream of the engineered site exhibited a steeper gradient of polarity. On monolayers of HEp-2 cells, the **SH**-minus virus produced syncytia which were at least equivalent in size to those of the wild type and produced plaques which were 70% larger. Furthermore, the **SH**-minus virus grew somewhat better (up to 12.6-fold) than wild-type recombinant **RSV** in certain cell lines. While the function of the **SH** protein remains to be determined, it seems to be

completely dispensable for growth in tissue culture and fusion function. When inoculated intranasally into mice, the **SH**-minus virus resembled the wild-type recombinant virus in its efficiency of replication in the lungs, whereas it replicated 10-fold less efficiently in the upper respiratory tract. In mice, the **SH**-minus and wild-type recombinant viruses were similarly **immunogenic** and effective in inducing resistance to virus challenge.

L6 ANSWER 18 OF 19 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1998062142 MEDLINE
DOCUMENT NUMBER: 98062142 PubMed ID: 9400970
TITLE: Recombinant vaccinia viruses expressing the **F**, **G** or N, but not the **M2**, protein of bovine **respiratory syncytial virus** (BRSV) induce resistance to BRSV challenge in the calf and protect against the development of pneumonic lesions.
AUTHOR: Taylor G; Thomas L H; Furze J M; Cook R S; Wyld S G; Lerch R; Hardy R; Wertz G W
CORPORATE SOURCE: Institute for Animal Health, Compton, Newbury, Berkshire, UK.. animal.health@bbsrc.ac.uk
CONTRACT NUMBER: AI 20181 (NIAID)
SOURCE: JOURNAL OF GENERAL VIROLOGY, (1997 Dec) 78 (Pt 12) 3195-206.
Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 19980122
Entered Medline: 19980105

AB The **immunogenicity** and protective efficacy of recombinant vaccinia viruses (rVV) encoding the **F**, **G**, N or **M2** (22K) proteins of bovine **respiratory syncytial virus** (BRSV) were evaluated in calves, the natural host for BRSV. Calves were vaccinated either by scarification or intratracheally with rVV and challenged 6 to 7 weeks later with BRSV. Although replication of rVV expressing the **F** protein in the respiratory tract was limited after intratracheal vaccination, the levels of serum and pulmonary antibody were similar to those induced following scarification. The serum antibody response induced by the **F** protein was biased in favour of IgG1 antibody, whereas the **G** and the N proteins induced similar levels of IgG1:IgG2, and antibody was undetectable in calves primed with the **M2** protein. The **F** protein induced neutralizing antibodies, but only low levels of complement-dependent neutralizing antibodies were induced by the **G** protein, and antibody induced by the N protein was not neutralizing. The **F** and N proteins primed calves for BRSV-specific lymphocyte proliferative responses, whereas proliferative responses were detected in calves primed with the **G** protein only after BRSV challenge. The **M2** protein primed lymphocytes in only one out of five calves. Although there were differences in the immune responses induced by the rVVs, the **F**, **G** and N, but not the **M2**, proteins induced significant protection against BRSV infection and, in contrast with the enhanced lung pathology seen in mice vaccinated with rVV expressing individual proteins of human (H)**RSV**, there was a reduction in lung pathology in calves.

L6 ANSWER 19 OF 19 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 1998055719 MEDLINE
DOCUMENT NUMBER: 98055719 PubMed ID: 9395341
TITLE: Structural properties of chimeric peptides containing a T-cell epitope linked to a fusion peptide and their importance for in vivo induction of cytotoxic T-cell responses.
AUTHOR: Lelievre D; Hsu S C; Daubos P; Favard C; Vigny P; Trudelle Y; Steward M W; Delmas A
CORPORATE SOURCE: Centre de Biophysique Moleculaire, UPR 4301 CNRS, Orleans, France.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1997 Nov 1) 249 (3) 895-904.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980115

AB We have previously shown that when administered to mice without adjuvant, a chimeric peptide consisting of the fusion peptide **F** from measles virus protein linked at the C-terminus of a cytotoxic T-cell epitope from the **M2** protein of **respiratory syncytial virus** efficiently primes for an major histocompatibility complex (MHC) class-I restricted cytotoxic T lymphocyte (CTL) response. In this report, we demonstrated by microspectrofluorometry that the fusion-peptide moiety bound to the plasma membrane of living cells. When the fusion peptide was linked to the C-terminus of the CTL epitope, the chimeric peptide (**M2-F**) adopted a marked beta-sheet conformation. In contrast, when the fusion peptide was linked to the N-terminus of the T-cell epitope (**F-M2**), the chimeric peptide adopted an alpha-helical conformation in the presence of trifluoroethanol. The **immunogenicity** of the two chimeric peptides for class-I restricted CTL was also significantly different, the one adopting the alpha-helical conformation being more **immunogenic**. Probably due to its obvious conversion to an alpha-helical conformation, the **F-M2** peptide could have a higher propensity to insert into membranes, as shown by microspectrofluorometry, with a resultant better **immunogenicity** than the **M2-F** peptide.

=> d ibib abs ind l9 1-2

L9 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:282424 HCAPLUS
DOCUMENT NUMBER: 138:286003
TITLE: DNA **vaccine** for respiratory syncytial virus
INVENTOR(S): Mohaptra, Shyam S.; **Kumar, Mukesh**; Huang, Shau-ku; **Leong, Kam W.**; Lockey, Richard F.; Zhang, Jian; Behera, Aruan K.; Chen, Li-chen; Perez De La Cruz, Ch
PATENT ASSIGNEE(S): University of South Florida, USA; Johns Hopkins University
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003028759	A1	20030410	WO 2002-US4114	20020212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003068333	A1	20030410	US 2002-73065	20020212

PRIORITY APPLN. INFO.: US 2001-325573P P 20010928

AB An effective prophylactic mucosal **gene expression vaccine** (GXV), made up of a cocktail of a least 4 different plasmid DNAs encoding corresponding RSV antigens, coacervated with chitosan to formulate nanospheres. In a murine model of RSV infection, intranasal administration with GXV results in significant induction of RSV-specific antibodies, nasal IgA antibodies, cytotoxic T lymphocytes, and IFN-.gamma. prodn. in the lung and splenocytes. A single dose of GXV induces a drastic redn. of viral titers.

IC ICM A61K039-155
ICS A61K047-36; C12N015-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 14, 63
ST respiratory syncytial virus DNA **vaccine**
IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(22,000-mol.-wt., M2; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)
IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A, secretory; to respiratory syncytial virus induced by DNA **vaccine** of plasmid vectors)
IT Human
(DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)
IT Human respiratory syncytial virus
(DNA **vaccine** of plasmids expressing antigens of)

IT Glycoproteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(F; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Glycoproteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(G; to respiratory syncytial virus induced by DNA **vaccine** of plasmid vectors)

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M (matrix); DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N (nucleocapsid); DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NS1 (nonstructural, 1); DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NS2 (nonstructural, 2); DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Phosphoproteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT T cell (lymphocyte)
(cytotoxic; to respiratory syncytial virus induced by DNA **vaccine** of plasmid vectors)

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophobic, SH (small hydrophobic); DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Respiratory tract, disease
(hyperresponsiveness; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus in relation to)

IT Development, mammalian postnatal
(infant; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus)

IT Respiratory tract, disease
(lower, infection; plasmid vectors expressing antigens of respiratory syncytial virus for vaccination against)

IT Drug delivery systems
(nanospheres; for plasmid vectors expressing antigens of respiratory syncytial virus)

IT **Vaccines**

(nasal; plasmids expressing antigens of respiratory syncytial virus)
IT Gene, microbial
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of respiratory syncytial virus antigens for DNA vaccination)
IT **Vaccines**
(oral; plasmids expressing antigens of respiratory syncytial virus)
IT Plasmid vectors
(pVAX; for expression of antigens of respiratory syncytial virus in DNA vaccination)
IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma.; DNA **vaccine** of plasmid vectors expressing antigens of respiratory syncytial virus induces prodn. of)
IT 9012-76-4, Chitosan
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanospheres; for delivery of plasmid vectors expressing antigens of respiratory syncytial virus)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:888800 HCAPLUS
DOCUMENT NUMBER: 137:389134
TITLE: Biodegradable polyphosphates for controlled release of drugs and genes and their preparation
INVENTOR(S): Wang, Jun; Mao, Hai-Quan; **Leong, Kam Weng**
PATENT ASSIGNEE(S): Johns Hopkins Singapore Pte. Ltd., Singapore
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092667	A1	20021121	WO 2002-SG90	20020514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-290888P P 20010514
AB The pos. chargeable polyphosphoester comprises .gtoreq.1 phosphoester linkage in the polymer backbone and .gtoreq.1 pos. chargeable group which is a substituent of a side chain attached to the polymer backbone through a phosphoester linkage. The polyphosphoester is prepd. by polymg. .gtoreq.1 monomer to form a polymer with .gtoreq.1 phosphoester linkage in polymer backbone, reacting the polymer with a alc. with a chargeable group or its substituents. The compns. contg. the polyphosphoesters and biol. active substances are useful for delivery of drugs and genes. A controlled gene delivery system based on these polyphosphoesters is prepd. by complex coacervation of nucleic acid (DNA or RNA) with the polymers.

The release rates can be manipulated by adjusting the charge ratios of polyphosphoesters to nucleic acids. This gene delivery system yields a higher **gene expression** in muscle when injected i.m.

IC ICM C08G079-04
ICS A61K047-48; A61P021-06; A61P011-06; A61P009-10; A61P001-08; A61P035-00; A61P011-02; A61P001-12; A61P001-10

CC 63-5 (Pharmaceuticals)

ST polyphosphoester carrier drug gene delivery

IT Animal cell line
(Hek 293; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Immunostimulants
(adjuvants; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphiphilic; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(biodegradable; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Drug delivery systems
(carriers; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Drug delivery systems
(controlled-release; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs.; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Polyphosphoric acids
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(esters; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Gene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT DNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasmid; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Drugs
Gene therapy
Human
Mammalia
Mouse
Primates
Vaccines
(prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Cytokines
DNA
Interleukin 10
Interleukin 12
Interleukin 4

Interleukin 5
Proteins
RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Therapy
(small mol.; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT 83906-57-4DP, chlorinated, esterified and hydrolyzed 83945-68-0DP, chlorinated, esterified and hydrolyzed
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT 77987-49-6DP, Benzyl N-(2-hydroxyethyl)carbamate, reaction products of chlorinated poly(4-methyl-2-hydro-1,3,2-dioxaphospholane)
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT 64-18-6, Formic acid, reactions 7782-50-5, Chlorine, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT 9031-11-2, .beta.-Galactosidase 191681-52-4, Sequence
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

IT 16352-26-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of biodegradable polyphosphates for controlled release of drugs and genes)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his ful

     (FILE 'HOME' ENTERED AT 15:56:41 ON 25 AUG 2003)

     FILE 'HCAPLUS' ENTERED AT 15:56:51 ON 25 AUG 2003
L1          4360 SEA ABB=ON  (RSV? OR ?RESPIRATOR?(W)?SYNCYTIAL?(W)?VIRUS?)
L2           187 SEA ABB=ON  L1 AND ?IMMUNOGEN?
L3           138 SEA ABB=ON  L2 AND (F OR G OR M OR SH OR NS1? OR NS2? OR P)
L4            13 SEA ABB=ON  L3 AND M2?  13 cits from CA Plus

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     16:06:55 ON 25 AUG 2003
L5            29 SEA ABB=ON  L4
L6            19 DUP REMOV L5 (10 DUPLICATES REMOVED)  19 cits from other databases
```

Please let me know if you'd like any revisions —

Mary Jane Ruhl